CHAPTER 43

Heart Murmurs: General Principles

KEY TEACHING POINTS

- Murmurs are classified by their timing (systolic, diastolic, or continuous), location, intensity, and frequency content (i.e., high frequency, low frequency, mixture of frequencies).
- Systolic murmurs result from abnormal flow over an outflow tract or semilunar valve (i.e., aortic or pulmonic valve) or from ventricular regurgitation into a low-pressure chamber (mitral or tricuspid regurgitation, or ventricular septal defect). Diastolic murmurs result from leakage of a semilunar valve (aortic or pulmonary regurgitation) or abnormal flow over an atrioventricular valve (mitral or tricuspid stenosis, flow rumbles).
- Practicing onomatopoeia (i.e., using the human voice to mimic murmurs) helps clinicians to correctly identify a murmur's timing and frequency content. In addition, rapid recognition of cadences of sounds becomes possible using onomatopoeia, thus avoiding the need to dissect auscultatory findings into their individual parts.
- The most helpful diagnostic finding in patients with systolic murmurs is the distribution of sound on the chest wall. Also helpful diagnostically are the intensity of S_1 and S_2, response of the murmur's intensity to changing cycle lengths (i.e., irregular beats), and the response to various maneuvers that affect venous return and afterload.

I. INTRODUCTION

Since the 1830s, the understanding of heart murmurs has evolved in three distinct stages.[1] In the first stage, brilliant clinicians——James Hope (1801–1841), Austin Flint (1812–1886), and Graham Steell (1851–1942)—attentively observed patients at the bedside and correlated the timing and quality of murmurs to the patients' clinical course and postmortem findings.[2] In the second stage, during the 1950s and 1960s, cardiac catheterization and phonocardiography helped clinicians to understand the hemodynamics responsible for heart murmurs,[3-5] and the introduction of cardiac surgery increased the stakes of cardiac auscultation, stimulating clinicians to be as precise and accurate as possible. Finally, in the 1970s and 1980s the introduction of echocardiography solved many of the remaining mysteries about murmurs, including the cause of ejection sounds in aortic stenosis and late systolic murmurs and clicks in mitral valve prolapse.

This chapter covers the principles of describing and diagnosing murmurs. Specific cardiac disorders and their associated murmurs are further discussed in Chapters 44 to 46.

II. THE FINDINGS

The important characteristics of heart murmurs are location (both where it is loudest and in which direction the sound travels, or *radiates*), timing, intensity, and frequency (or *pitch*, which is high, low, or a mixture of high and low frequencies).[6] The terms *rough*, *rumbling*, *blowing*, *coarse*, and *musical* are also sometimes used to describe the specific tonal quality of murmurs.

Murmurs frequently vary in intensity during the respiratory cycle, but loud murmur-like sounds that completely disappear during inspiration or expiration are likely pericardial rubs, not murmurs.[7]

A. BASIC CLASSIFICATION OF MURMURS

Murmurs are broadly classified as systolic, diastolic, and continuous (Table 43.1).[6] **Systolic murmurs** occur during the time between S_1 and S_2; **diastolic murmurs** occur at any time from S_2 to the next S_1. **Continuous murmurs** begin in systole but extend beyond S_2 into diastole, indicating they do not respect the confines of systole and diastole and thus arise *outside* the four heart chambers. Despite the name, continuous murmurs do not necessarily occupy all of systole and diastole.

1. SYSTOLIC MURMURS

A. ETIOLOGY

There are two causes of systolic murmurs.

(1). ABNORMAL FLOW OVER AN OUTFLOW TRACT OR SEMILUNAR VALVE. One cause is abnormal flow over an outflow tract or semilunar valve (i.e., aortic or pulmonary valve), such as: (1) forward flow across an obstruction (e.g., aortic stenosis, pulmonic stenosis, or hypertrophic cardiomyopathy), or (2) increased flow across a normal semilunar valve (e.g., atrial septal defect or the flow murmurs of anemia, fever, pregnancy, or thyrotoxicosis).

(2). REGURGITATION FROM A VENTRICLE INTO A LOW PRESSURE CHAMBER. Examples are mitral regurgitation (leak between left ventricle and left atrium), tricuspid regurgitation (leak between right ventricle and right atrium), and ventricular septal defect (leak between left and right ventricles).

B. OLDER CLASSIFICATIONS OF SYSTOLIC MURMURS: "EJECTION" AND "REGURGITATION" MURMURS

In 1958 Leatham divided all systolic murmurs into "ejection murmurs" and "regurgitant murmurs," based entirely on their relationship to S_2.[3,4] According to his classification, ejection murmurs begin after S_1, have a crescendo-decrescendo shape, and always end before S_2.* Ejection murmurs represent abnormal flow across the aortic or pulmonic valve. In contrast, regurgitant murmurs (e.g., mitral and tricuspid regurgitation) begin with S_1, have a plateau shape, and extend up to S_2 or even slightly past it (thus obliterating S_2).

Leatham's classification is no longer widely used for several reasons: (1) It relies entirely on phonocardiography and does not always correspond to what clinicians hear at the bedside.[8] (2) It depends entirely on the audibility of the aortic and pulmonary components of S_2, sounds that sometimes are inaudible. (3) It assumes all ejection murmurs result from ejection over a semilunar valve, although experience

*More precisely, "ejection" murmurs end before the S_2 component belonging to the side of the heart generating the murmur. For example, the murmur of aortic stenosis ends before A_2; the murmur of pulmonic stenosis ends before P_2.

TABLE 43.1 Classification of Murmurs by Timing and Location

Type of Murmur	Location Where Loudest
SYSTOLIC MURMURS	
Abnormal Flow Over Outflow Tract or Semilunar Valve	
Aortic stenosis	R base, LLSB, and apex
Pulmonic stenosis	L base
Atrial septal defect*	L base
Hypertrophic cardiomyopathy with obstruction	LLSB
Regurgitation From High-Pressure Chamber into Low-Pressure Chamber	
Mitral regurgitation	Apex
Tricuspid regurgitation	LLSB
Ventricular septal defect	LLSB
DIASTOLIC MURMURS	
Backward Flow Across Leaking Semilunar Valve	
Aortic regurgitation	LLSB
Pulmonary regurgitation	L base
Abnormal Forward Flow Over an Atrioventricular Valve	
Mitral stenosis	Apex
Tricuspid stenosis	LLSB
CONTINUOUS MURMURS	
Abnormal Connections Between Artery and Vein	
Patent ductus arteriosus	L base
Arteriovenous fistula	Over fistula
Abnormal Flow in Veins	
Venous hum	Above head of clavicle
Mammary souffle†	Between breast and sternum
Stenosis in Peripheral Artery	
Coarctation of the aorta	Over back

*The murmur of atrial septal defect is due to excess flow of blood over the pulmonary valve (from left-to-right shunting), not from flow through the defect itself.
†"Souffle" (French for "sound" or "murmur") is pronounced *SOO-ful*.
Apex, Point of apical impulse; *L base*, second left intercostal space next to sternum; *LLSB*, fourth and fifth left intercostal space next to sternum; *R base*, second right intercostal space next to sternum.

has shown many are due to regurgitant lesions. (4) Its fundamental premise, that the intensity of a murmur depends on pressure gradients, is not always true (e.g., the murmur of mitral valve prolapse is loudest during late systole, when gradients are decreasing).

Instead, systolic murmurs are more easily classified using onomatopoeia as mid-systolic, early systolic, long systolic, holosystolic, and late systolic, based only on whether the murmur obscures S_1, S_2, or both sounds (see the section on Timing and Quality of Murmurs Using Onomatopoeia).[1]

2. DIASTOLIC MURMURS

There are two causes of diastolic murmurs: (1) abnormal backward flow across a leaking semilunar valve (e.g., aortic or pulmonic regurgitation) or (2) abnormal

forward flow across an atrioventricular valve (e.g., mitral stenosis, tricuspid stenosis, and flow rumbles[†]).

3. CONTINUOUS MURMURS

Continuous murmurs result from the following: (1) abnormal connections between the aorta and pulmonary trunk (e.g., patent ductus arteriosus), (2) abnormal connections between arteries and veins (e.g., arteriovenous fistulas) (see Chapter 54), (3) abnormal flow in veins (e.g., venous hum and mammary souffle), or (4) abnormal flow in arteries (e.g., coarctation of the aorta, renal artery stenosis).

B. LOCATION ON THE CHEST WALL

The usual locations of conventional murmurs are described in Table 43.1. Nonetheless, in patients with systolic murmurs, one of the most helpful diagnostic signs is the distribution of the sound on the chest wall with reference to the third left parasternal space, a landmark that lies directly over both the aortic and mitral valves and distinguishes systolic murmurs into one of six possible patterns: (1) broad apical-base pattern; (2) small apical-base pattern; (3) left lower sternal pattern; (4) broad apical pattern; (5) isolated apical pattern; and (6) isolated base pattern (definitions of these patterns appear in Fig. 43.1).[7]

Inspection of the boundary surrounding all six patterns suggests the primary determinant of a murmur's radiation is not necessarily the direction of blood flow but instead the orientation of bony thorax, specifically the left lower ribs, sternum, and clavicles (Fig. 43.2). Increased flow across a semilunar valve or through a regurgitant leak generates vibrations in the ventricles, great arteries, or both, which—depending on their location, amplitude, and ease of conduction to the bones of the body wall—produce one of the six different murmur patterns. Indeed, one of the best arguments that bone conduction—and not direction of blood flow—governs distribution of sound is the murmur of mitral regurgitation: in this lesion blood flows from the left ventricle *rightward* and *upward* to the left atrium, yet the murmur radiates almost perpendicular to this, along the left lower ribs to the axilla.[7]

The diagnostic significance of these six systolic murmur patterns is discussed in the section on Differential Diagnosis of Systolic Murmurs.

C. SPECIFIC TIMING AND QUALITY OF MURMURS USING ONOMATOPOEIA

Fig. 43.3 presents traditional diagrams of various heart murmurs, which in turn are based on phonocardiographic tracings. However, because murmurs are sounds, diagrams such as these often fail to convey the precise cadence and tonal qualities that distinguish murmurs. Throughout the history of cardiac auscultation, clinicians have used onomatopoeia to mimic heart sounds and murmurs, finding this to be an effective teaching tool allowing clinicians to rapidly recognize the patterns of different sounds.[2,9,10]

The system described here is based on the published work of Feinstein[11] and Adolph.[12-15] High-frequency murmurs are mimicked by sounds from the front of the

[†]Flow rumbles are short low-frequency diastolic murmurs that result from increased flow over a nonobstructed atrioventricular valve. Atrial septal defects and tricuspid regurgitation increase diastolic flow over the tricuspid valve and may cause tricuspid flow rumbles (which resemble the murmur of tricuspid stenosis). Mitral regurgitation and ventricular septal defect increase diastolic flow over the mitral valve and may produce mitral flow rumbles (which resemble the murmur of mitral stenosis).

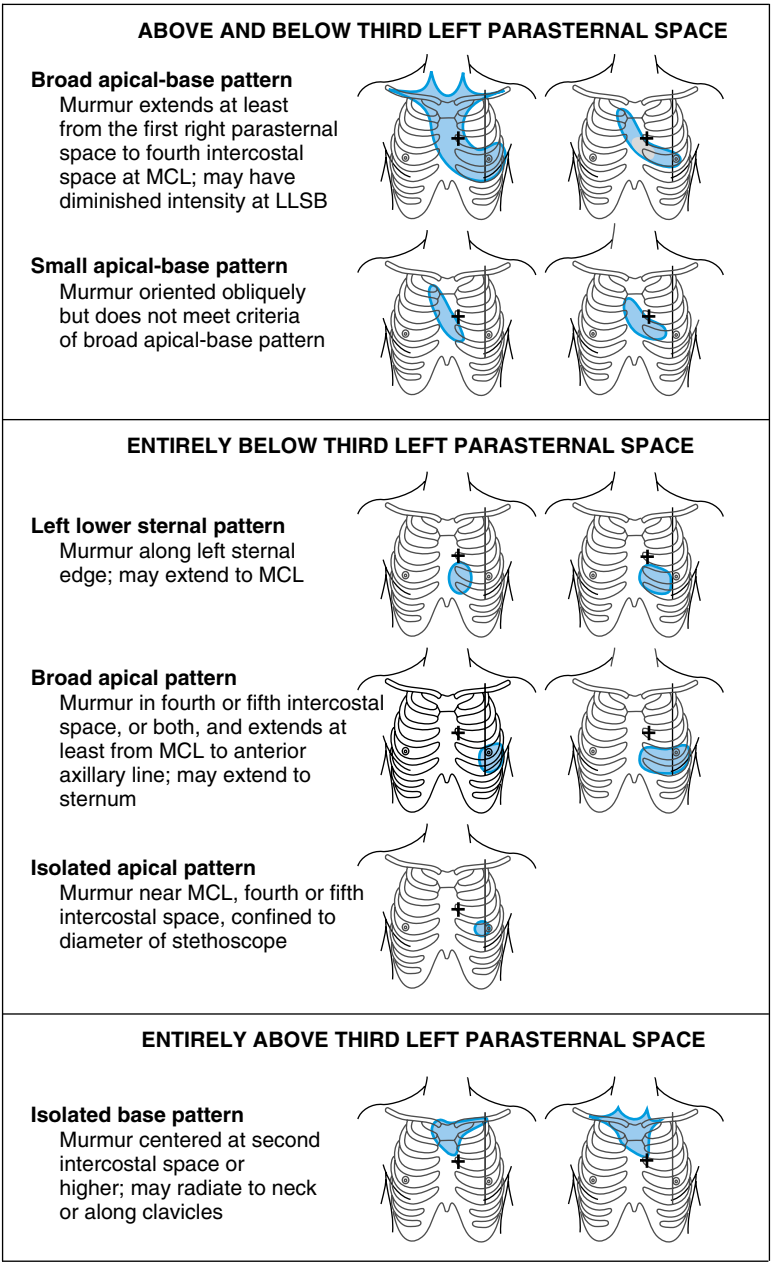

FIG. 43.1 SIX SYSTOLIC MURMUR PATTERNS. Each of the six topographic patterns are distinguished by their distribution with reference to the third left parasternal space (indicated by "+" symbol in each drawing). This landmark is easily identified by first identifying the sternal angle, where the second rib articulates, and then counting down to the second ICS, third rib, and then the third parasternal space. Two of the patterns traverse above and below this landmark (*broad apical-base* and *small apical-base* patterns); three are confined below this landmark (*left lower sternal*, *broad apical*, and *isolated apical* patterns); and one is confined entirely above the landmark (*isolated base* pattern). *ICS*, Intercostal space; *LLSB*, left lower sternal border; *MCL*, midclavicular line. Based upon reference 7.

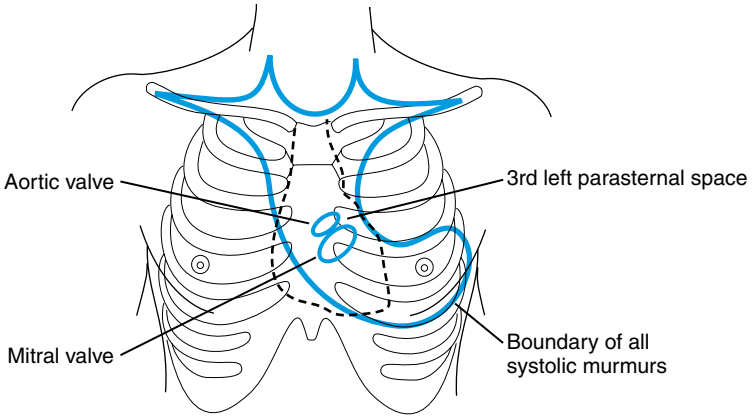

FIG. 43.2 BOUNDARY OF SYSTOLIC MURMUR PATTERNS. The third left parasternal space overlies both the aortic and mitral valves. If the ventricles vibrate sufficiently to produce sound, murmurs are generated below this landmark. Vibrations of the right ventricle produce the *left lower sternal* pattern, whereas those of the left ventricle produce the *isolated apical* pattern or *broad apical* pattern. Should the great arteries vibrate sufficiently to make sound, the bones above this landmark vibrate and murmurs radiate from the upper sternum to clavicles and neck (*isolated base* pattern). With increased velocity across the aortic valve, both the left ventricle (lower ribs) and great arteries (upper sternum and clavicles) vibrate, causing the *apical-base pattern* and its variations. Based upon reference 7.

mouth; low-frequency murmurs are mimicked by sounds from the back of the throat. The high-frequency murmur of mitral and tricuspid regurgitation is mimicked by saying SHSHSHSH. The high-frequency murmur of aortic regurgitation is mimicked by blowing air out through slightly pursed lips, or whispering PHEWEWEWEWEW or AHAHAHAHAH (hence the "blowing" descriptor). The low-frequency murmurs of tricuspid or mitral stenosis are mimicked by the "RRRRR" portion of a growl (hence the "rumbling" descriptor). Murmurs containing a mixture of low and high frequencies, such as aortic stenosis, are mimicked by the sound made when clearing the throat (common descriptors are "coarse" or "harsh").

The clinician should first establish the normal cadence of S_1 and S_2 (*lub* is S_1 and *dup* is S_2):

lub dup *lub dup* *lub dup*

Then, the murmur is added at the appropriate time. For example, the high-frequency late systolic murmur of mitral valve prolapse preserves S_1 but obscures S_2 (i.e., *dup* is replaced by *SHSHP*):

lub SHSHP *lub SHSHP* *lub SHSHP*

Table 43.2 describes how to label the timing of systolic murmurs, and Fig. 43.4 shows how onomatopoeia can mimic many common murmurs.

By using onomatopoeia, clinicians can quickly learn the cadence of murmurs, which sometimes leads to rapid recognition of complicated sounds without first having to sort out the location of S_1 and S_2. For example, if auscultation reveals a cadence consisting of a single murmur and no heart sounds,

SHSHSHP *SHSHSHP* *SHSHSHP*

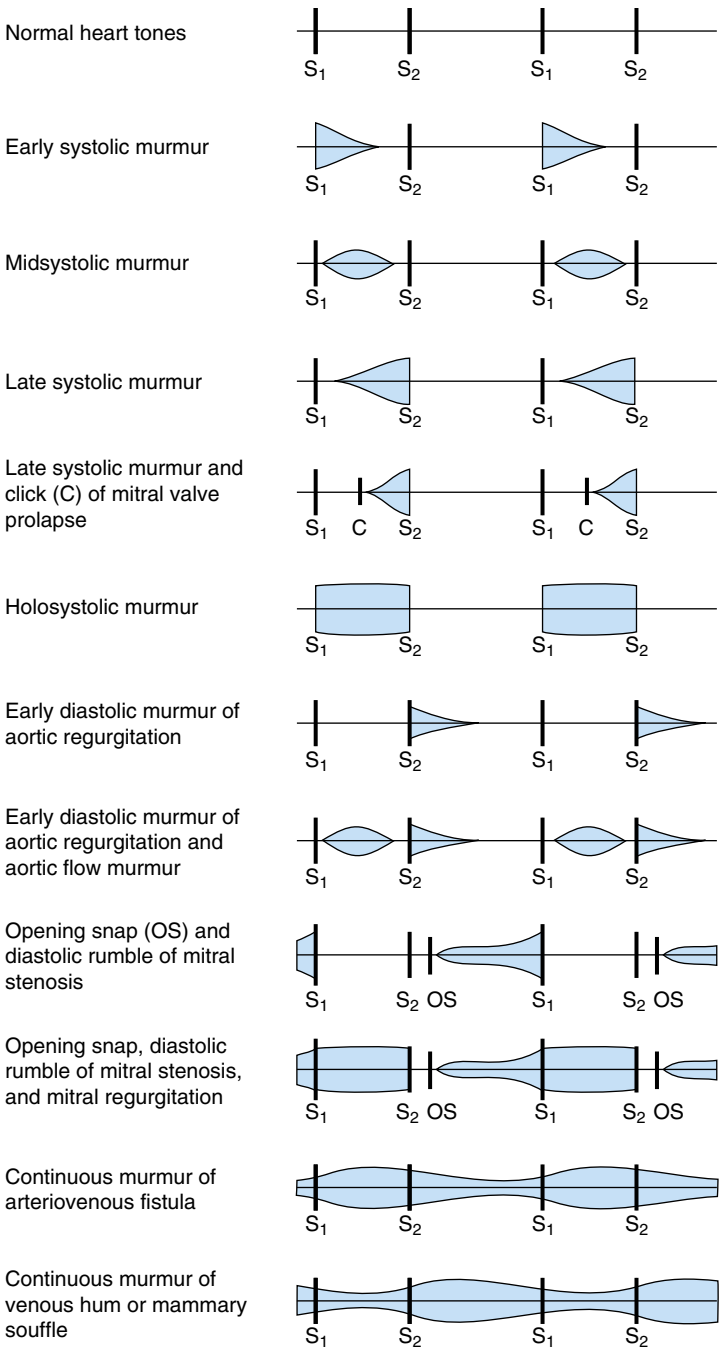

FIG. 43.3 DIAGRAMS OF VARIOUS MURMURS.

TABLE 43.2 Using Onomatopoeia to Identify Systolic Murmur Timing

Onomatopoeia	Definition	Timing of Murmur
Lub shsh dup	Both S_1 (*lub*) and S_2 (*dup*) distinct:	Midsystolic
Shshsh dup *Pushsh dup*	S_1 indistinct, S_2 distinct; gap before S_2	Early systolic
Shshshshdup *Pushshshdup*	S_1 indistinct, S_2 distinct; no gap before S_2	Long systolic
Shshshshshsh *ShshshshshshP* *Pushshshshsh* *PushshshshshP*	S_1 and S_2 indistinct	Holosystolic
Lub shshshP	S_1 distinct, S_2 indistinct	Late systolic

Based upon reference [7].

the only possible diagnosis is a holosystolic murmur.

If auscultation reveals murmurs in both systole and diastole, there are three possible causes: (1) a true continuous murmur, (2) a to-fro murmur, or (3) combined mitral stenosis and regurgitation. In **true continuous murmurs** the cadence is uninterrupted by the cardiac cycles ("*SHSHSHSHSHSHSHSH*"). **To-fro murmurs** consist of two high-frequency murmurs, one in systole and another in diastole ("*SHSHSHSHP PHEWEWEWEWEW*"). To-fro murmurs result from isolated severe aortic regurgitation (the diastolic component representing aortic regurgitation and the systolic one representing increased systolic flow over the aortic valve) or aortic regurgitation combined with another systolic murmur, such as aortic stenosis, mitral regurgitation, or ventricular septal defect. In combined mitral stenosis and regurgitation, a high-frequency murmur is combined with a low-frequency one ("PUSHSHSHSHP DUPRRRRRRRRUP").

D. GRADING THE INTENSITY OF MURMURS

The intensity of murmurs is graded on a 1 to 6 scale, based on the work of Freeman and Levine, which was later modified by Constant and Lippschutz (their work is now collectively referred to as the **Levine grading system**).[16-18] Although this system was devised for systolic murmurs, it is often applied to all murmurs.

The six categories are: (1) **Grade 1 murmurs** are so faint they can be heard only with special effort. (2) **Grade 2 murmurs** can be recognized readily after placing the stethoscope on the chest wall. (3) **Grade 3 murmurs** are very loud. (Murmurs of grades 1 through 3 all lack thrills, which are palpable vibrations on the body wall resembling the purr of a cat. Murmurs of grades 4 through 6 have associated thrills.) (4) **Grade 4 murmurs** are very loud, although the stethoscope must be in complete contact with the skin to hear them. (5) **Grade 5 murmurs** are very loud and still audible if only the edge of the stethoscope is in contact with the skin; they are not audible after complete removal of the stethoscope from the chest wall. (6) **Grade 6 murmurs** are exceptionally loud and audible even when the stethoscope is just removed from the chest wall.

Normal heart tones	**Lub** **Dup** S_1 S_2	**Lub** **Dup** S_1 S_2
Early systolic murmur	**L**SHSHSH **Dup** S_1 S_2	**L**SHSHSH **Dup** S_1 S_2
Midsystolic murmur	**Lub** SHSH **Dup** S_1 S_2	**Lub** SHSH **Dup** S_1 S_2
Late systolic murmur	**Lub** SHSH**P** S_1 S_2	**Lub** SHSH**P** S_1 S_2
Late systolic murmur and click (C) of mitral valve prolapse	**Lub** **K**SHSH**P** S_1 C S_2	**Lub** **K**SHSH**P** S_1 C S_2
Holosystolic murmur	SHSHSHSHSH S_1 S_2	SHSHSHSHSH S_1 S_2
Early diastolic murmur of aortic regurgitation	**Lub** **P**EWWWww S_1 S_2	**Lub** **P**EWWWww S_1 S_2
Early diastolic murmur of aortic regurgitation and aortic flow murmur	**Lub** SHSH **P**EWWWww S_1 S_2	**Lub** SHSH **P**EWWWww S_1 S_2
Opening snap (OS) and diastolic rumble of mitral stenosis	RU**P** bu **DUP**RRRRRRU**P** S_1 S_2 OS	bu **DUP**RRRRRRU**P** S_1 S_2 OS
Opening snap, diastolic rumble of mitral stenosis, and mitral regurgitation	RU**P**SHSHSHS**P** **DUP**RRRRRRU**P**SHSHSHS**P** **DUP**RRRRRRU**P** S_1 S_2 OS	S_1 S_2 OS
Continuous murmur of arteriovenous fistula	**Pu**SHSHSH**PuS**HSHSHSHSH **Pu**SHSHSH**PuS**HSHSHSHSH S_1 S_2	S_1 S_2
Continuous murmur of venous hum or mammary souffle	**Pu**SHSHSHS**Pu**SHSHSHSHSH **Pu**SHSHSHS**Pu**SHSHSHSHSH S_1 S_2	S_1 S_2

FIG. 43.4 MURMURS AND ONOMATOPOEIA.

III. CLINICAL SIGNIFICANCE

A. DETECTING VALVULAR HEART DISEASE

In EBM Box 43.1, a *characteristic* murmur refers to the expected murmur of the specific lesion (as described in Table 43.1 and Chapters 44 to 46). For example, in the detection of aortic regurgitation, a characteristic murmur refers to an early diastolic high-frequency murmur along the lower sternal border, not just any diastolic murmur. In these studies, trivial regurgitation (a common finding at echocardiography of no clinical significance) was classified as "no regurgitation" (i.e., "no disease").

For five of the lesions in EBM Box 43.1, the finding of the characteristic murmur is a conclusive argument that that lesion is present: tricuspid regurgitation (likelihood ratio [LR] = 14.6; see EBM Box 43.1), ventricular septal defect (LR = 24.9), mitral valve prolapse (LR = 12.1), aortic regurgitation (LR = 9.9), and pulmonary regurgitation (LR = 17.4). For two murmurs, aortic stenosis and mitral regurgitation, the positive LRs are less compelling (LRs = 5.4 to 5.9), primarily because these two murmurs may be confused with each other and other systolic murmurs (see the section on Differential Diagnosis of Systolic Murmur).

The *absence* of the characteristic murmur *decreases* the probability of significant left-sided valvular lesions: aortic stenosis (negative LR = 0.1), moderate-to-severe mitral regurgitation (negative LR = 0.3), and moderate-to-severe aortic regurgitation (negative LR = 0.1) but does not exclude significant right-sided valvular lesions (the negative LRs for tricuspid regurgitation and pulmonary regurgitation are not significant), probably because pressures on the right side of the heart are lower and thus generate less turbulence and sound than left-sided pressures. Many patients with *mild* mitral regurgitation or *mild* aortic regurgitation also lack murmurs.

B. DIFFERENTIAL DIAGNOSIS OF SYSTOLIC MURMURS

Systolic murmurs are common bedside findings, occurring in 5% to 52% of young adults and 29% to 60% of older persons.[34] More than 90% of younger adults and more than half of older adults with systolic murmurs have normal echocardiograms, which means the murmur is "innocent" or "functional."[34]

1. THE FUNCTIONAL MURMUR

Functional murmurs are short, early or midsystolic murmurs of grade 2 of 6 or less that are well localized to the area of the left sternal border and diminish in intensity when the patient stands, sits up, or strains during the Valsalva maneuver. Patients with functional murmurs have normal neck veins, apical impulse, arterial pulse, and heart tones. The finding of a functional murmur in a patient increases the probability that the echocardiogram is normal (LR = 4.7; see EBM Box 43.1).

2. IDENTIFYING THE CAUSE OF SYSTOLIC MURMURS

In patients with abnormal systolic murmurs (i.e., murmurs that are *not* functional) the most important causes are increased aortic velocity (from aortic stenosis or increased flow over an unobstructed valve), mitral regurgitation, and tricuspid regurgitation. In patients with abnormal systolic murmurs, the most important features are distribution of sound on the chest wall (i.e., murmur pattern); intensity of S_1 and S_2; timing, radiation, and quality of sound; murmur intensity during irregular rhythms; and response to maneuvers.

EBM BOX 43.1
*Murmurs and Valvular Heart Disease**

Finding (Reference)†	*Sensitivity (%)*	*Specificity (%)*	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Functional Murmur				
Detecting normal findings on echocardiography[19,20]	67-98	70-91	**4.7**	NS
Characteristic Systolic Murmur				
Detecting mild or worse aortic stenosis[7]	90	85	**5.9**	**0.1**
Detecting severe aortic stenosis[7,21,22]	83-98	71-76	**3.5**	**0.1**
Detecting mild mitral regurgitation or worse[23,24]	56-75	89-93	**5.4**	0.4
Detecting moderate-to-severe mitral regurgitation[7,23,24]	73-93	61-76	2.6	**0.3**
Detecting mild tricuspid regurgitation or worse[24]	23	98	**14.6**	0.8
Detecting moderate-to-severe tricuspid regurgitation[7,24]	20-62	94-98	**9.6**	NS
Detecting ventricular septal defect[20]	90	96	**24.9**	NS
Detecting mitral valve prolapse[20]	55	96	**12.1**	0.5
Characteristic Diastolic Murmur				
Detecting mild aortic regurgitation or worse[24-31]	54-87	75-98	**9.9**	**0.3**
Detecting moderate-to-severe aortic regurgitation[24,29-31]	88-98	52-88	**4.3**	**0.1**
Detecting pulmonary regurgitation[24]	15	99	**17.4**	NS

*Diagnostic standard: for all *valvular lesions*, Doppler echocardiography,[7,20,24,29,32] angiography,[22,23,25-27,30,31,33] or surgery.[21,28] Echocardiographic trivial regurgitation is classified as "absent regurgitation" (i.e., no disease).

†Definition of findings: for *functional murmur*, see text; for all other *murmurs*, the murmur characteristic in quality, location, and timing for that specific diagnosis. For example, the positive LR of 9.9 for aortic regurgitation refers to an early diastolic high-frequency blowing decrescendo murmur at the lower left sternal border, not any diastolic murmur.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, Not significant.

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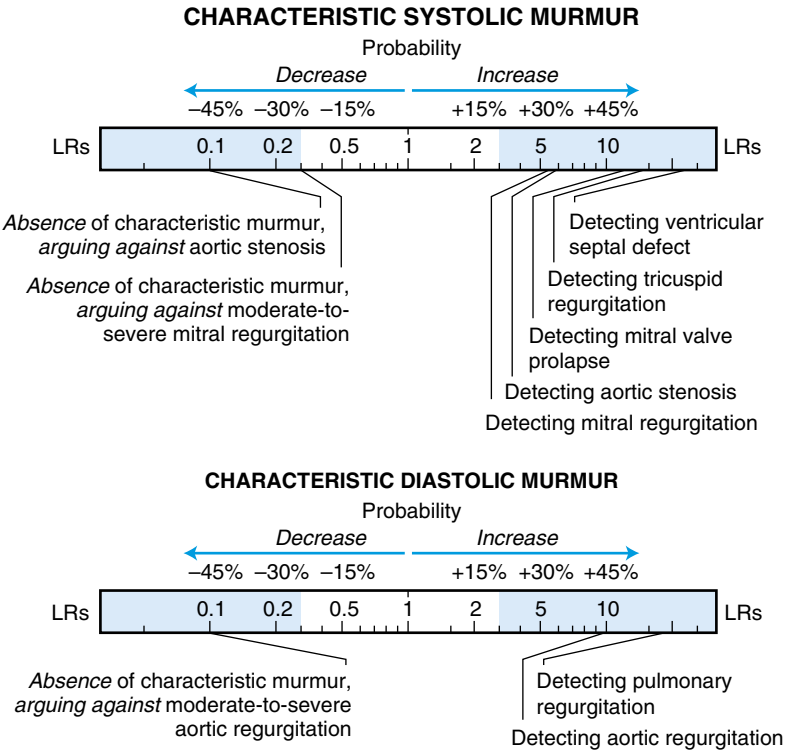

A. DISTRIBUTION OF MURMUR (MURMUR PATTERN; SEE FIG. 43.1)

EBM Box 43.2 indicates that one of the most important diagnostic signs is the distribution of sound on the chest wall. The broad apical-base pattern increases the probability of aortic stenosis (LR = 9.7; see EBM Box 43.2), the broad apical pattern increases the probability of mitral regurgitation (LR = 6.8), and the left lower sternal pattern increases the probability of tricuspid regurgitation (LR = 8.4).

In one study the small apical-base pattern was due to mildly increased aortic velocity (but aortic stenosis was rare); the isolated base pattern usually stemmed from increased flow in the great arteries, not the heart (e.g., anemia, hemodialysis fistula, or subclavian stenosis); and the isolated apical pattern was nondiagnostic.[7]

B. INTENSITY OF S_1 AND S_2

If S_1 intensity is determined at the apex and S_2 intensity at the left second parasternal space, and intensity is divided into four levels—inaudible, soft, normal, or loud—the finding of an inaudible S_1 (LR = 5.1; see EBM Box 43.2) or inaudible S_2 (LR = 12.7) in patients with systolic murmurs increases the probability of aortic stenosis, whereas the finding of a loud S_2 increases the probability of mitral regurgitation (LR = 4.7).

EBM BOX 43.2
Differential Diagnosis of Systolic Murmurs in Adults[*](7)*

Finding[†]	Likelihood Ratio for Detecting: *AV Peak Velocity ≥2.5 m/s*[‡]	*Mitral Regurgitation*	*Tricuspid Regurgitation*
Murmur Pattern			
Broad apical-base pattern	**9.7**	NS	NS
Broad apical pattern	**0.2**	**6.8**	2.5
LLSB pattern	NS	NS	**8.4**
Heart Tones[†]			
S_1 inaudible, apex	**5.1**	NS	NS
S_2 inaudible	**12.7**	NS	NS
S_2 loud	NS	**4.7**	**3.6**
Murmur Quality, Timing, and Intensity			
Radiation to neck	2.4	0.6	0.6
Timing midsystolic or early systolic	0.4	0.4	0.5
Timing long systolic or holosystolic	2.2	1.9	1.7
Coarse quality	**3.3**	0.5	0.5
If pulse irregular, murmur intensity same in beat after a pause	0.4	2.5	2.3

*Diagnostic standard: for all *valvular lesions*, Doppler echocardiography;[7] regurgitation severity is moderate or worse.

[†]Definition of findings: for *murmur pattern*, see Fig. 43.1; for *heart tones*, S_1 intensity is determined at the apex, S_2 intensity is determined at the left second parasternal space, and intensity graded into four levels, as inaudible, soft, normal, or loud; for *quality* and *timing*, see the section on Specific Timing and Quality of Murmurs Using Onomatopoeia in text and Table 43.2.

[‡]AV peak velocity ≥2.5 m/s indicates aortic stenosis, mild or worse.

AV, Aortic valve; *NS*, not significant.

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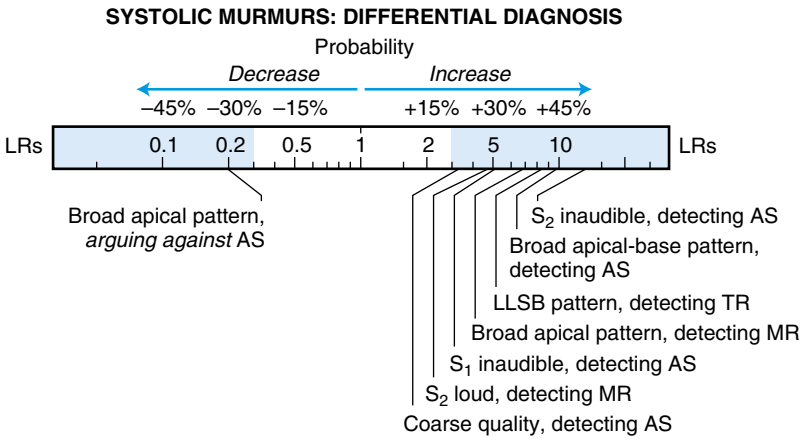

C. TIMING, RADIATION, AND QUALITY OF SOUND (SEE ALSO THE SECTION ON SPECIFIC TIMING AND QUALITY OF MURMURS USING ONOMATOPOEIA)

Pathologic murmurs have longer duration (long systolic or holosystolic, LRs 1.7 to 2.2) than nonpathologic ones. Most late systolic murmurs are due to mitral regurgitation.[7] Radiation into the neck (LR = 2.4) and coarse quality (LR = 3.3) increase the probability of aortic stenosis.

D. INTENSITY OF SYSTOLIC MURMUR DURING IRREGULAR RHYTHMS

One important clue to the etiology of a systolic murmur is how it changes in intensity with changing cycle lengths, as occurs in the irregular pulse of atrial fibrillation or frequent premature beats. Mitral regurgitation maintains the same intensity whether the beats are quick or delayed.[35] In contrast, the intensity of aortic stenosis depends on cycle length: the longer the previous diastole (e.g., beat after a premature beat or after a pause in atrial fibrillation), the louder the murmur.[35,36]

Explaining why these two murmurs behave differently first requires an understanding of the physiology of the pause (Fig. 43.5). The pause causes diastolic filling and contractility to be greater for the next beat than it would have been if the cycle had been quicker (contractility is increased because of Starling forces and, in the case of extrasystoles, postextrasystolic accentuation of contractility). The pause also reduces afterload for the next beat because the aortic pressures have had more time to decrease before the next ventricular systole. In aortic stenosis, all three of these changes—increased filling, increased contractility, and decreased afterload—promote greater flow across the stenotic valve after pauses than after quick beats,

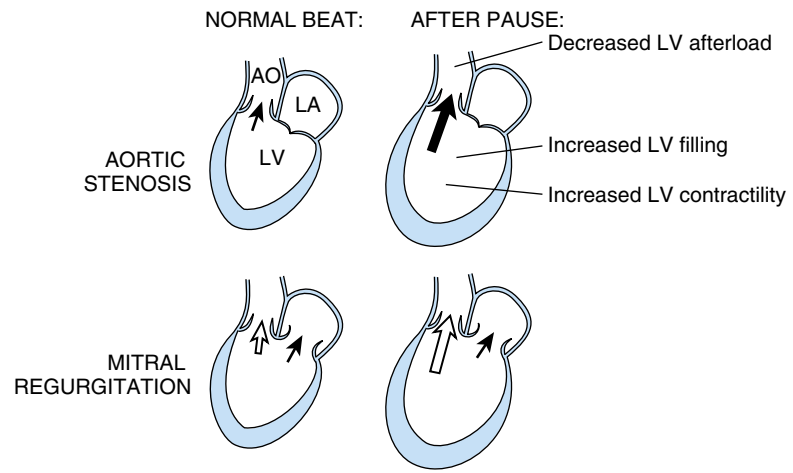

FIG. 43.5 INTENSITY OF SYSTOLIC MURMURS AND IRREGULAR RHYTHMS. The figure depicts blood flow and intensity of systolic murmurs during normal beats (*left column*) and after pauses in the heart rhythm (from extrasystoles or atrial fibrillation, *right column*). In each drawing the size of the arrow indicates the volume of blood flow: *black arrows* depict flow *causing* sound, whereas *open arrows* depict flow *not generating* sound. After the pause (*right column*), there is increased LV filling and contractility but *decreased* LV afterload. In aortic stenosis (*top rows*) these changes all favor increased flow across the aortic valve and a louder murmur (i.e., dark arrow is larger after the pause). In mitral regurgitation these same forces again favor increased flow across the aortic valve (*open arrow*), but because this flow is not generating sound, the regurgitant volume (*dark arrow*) and murmur intensity remains unchanged. See the text. *Ao,* Aorta; *LA*, left atrium; *LV*, left ventricle.

causing the murmur to become louder.[37] However, in mitral regurgitation the stroke volume is divided between two paths: (1) blood flowing out the aorta and (2) blood flowing into the left atrium. The reduced afterload promotes the extra filling from the pause to exit into the aorta, leaving the regurgitant volume the same as with quicker beats and making the intensity of the murmur independent of cycle length.

In one study, unchanging intensity of systolic murmurs during irregular rhythms increased the probability of regurgitation (LR = 2.5; see EBM Box 43.2).

Another systolic murmur, hypertrophic cardiomyopathy, responds unpredictably to changing cycle lengths: the long pause may make the murmur louder or softer or may not change it at all.[36]

E. MANEUVERS

Several maneuvers help to differentiate systolic murmurs (Table 43.3). They are classified into respiratory maneuvers, maneuvers that change venous return (e.g., Valsalva maneuver, squatting-to-standing, standing-to-squatting, passive leg

TABLE 43.3 Maneuvers and Heart Murmurs

Maneuver*	Technique	When to Note Change in Murmur
Respiration	The patient breathes normally in and out	During inspiration and expiration
MANEUVERS AFFECTING VENOUS RETURN		
Decrease Venous Return		
Valsalva maneuver	The patient exhales against closed glottis for 20 s	At end of the strain phase (i.e., at 20 s)
Squatting-to-standing	The patient squats for at least 30 s and then rapidly stands up	Immediately after standing
Increase Venous Return		
Standing-to-squatting	The patient squats rapidly from the standing position, while breathing normally to avoid a Valsalva maneuver	Immediately after squatting
Passive leg elevation	The patient's legs are passively elevated to 45 degrees while the patient is supine	15-20 s after leg elevation
MANEUVERS AFFECTING SYSTEMIC VASCULAR RESISTANCE (AFTERLOAD)		
Increase Afterload		
Isometric hand grip exercise	The patient uses one hand to squeeze the examiner's index and middle fingers together tightly†	After one minute of maximal contraction
Transient arterial occlusion	The examiner places blood pressure cuffs around both upper arms of patient and inflates them to pressures above the patient's systolic blood pressure	20 s after cuff inflation
Decrease Afterload		
Amyl nitrite	The patient takes three rapid deep breaths from an opened amyl nitrite capsule	15-30 s after inhalation

*Squatting-to-standing also decreases systemic vascular resistance, and amyl nitrite also diminishes pulmonary vascular resistance a small amount.
†In clinical studies a hand dynamometer was used to confirm that at least 75% of maximal handgrip strength was sustained for 1 min.[38]
From information cited in references 37-41.

elevation), and maneuvers that primarily change systemic vascular resistance (isometric hand grip, transient arterial occlusion, and inhalation of amyl nitrite).

(1). RESPIRATION. Inspiration increases venous return to the right side of the heart and decreases it to the left side of the heart.‡ Therefore murmurs that intensify during inspiration characteristically originate in the right side of the heart (e.g., tricuspid regurgitation or pulmonic stenosis; LR = 7.8; EBM Box 43.3). Murmurs that become *softer* during inspiration are most likely *not* right-sided murmurs (LR = 0.2).

Before interpreting the test, however, the clinician should be certain the patient is breathing evenly in and out because irregular breathing or breath-holding makes interpretation impossible. To help to direct the patient's breathing, the clinician can move his or her arm slowly up and down and ask the patient to breathe in when the arm is going up and out when it is going down.

Inspiratory intensification of the murmur of tricuspid regurgitation was originally described by Rivero-Carvallo in 1946 (the sign is sometimes called **Carvallo sign**).[46]

(2). MANEUVERS CHANGING VENOUS RETURN. Venous return to the heart *decreases* during the straining phase of the Valsalva maneuver and the squatting-to-standing maneuver. Venous return *increases* during passive leg elevation and the standing-to-squatting maneuver (see Table 43.3 for definitions).

These maneuvers are most useful in identifying hypertrophic cardiomyopathy, which, unlike most systolic murmurs, intensifies with decreased venous return and becomes softer with increased venous return. This paradoxical response occurs because the murmur is caused by obstruction in the outflow tract, below the aortic valve and between the anterior leaflet of the mitral valve and the hypertrophied interventricular septum. Decreased venous return brings the mitral leaflet and septum closer together and aggravates the obstruction; increased return moves them apart and relieves the obstruction.

All four venous return maneuvers are useful in diagnosing hypertrophic cardiomyopathy (LRs = 6 to 14; see EBM Box 43.3), although intensification of the murmur during Valsalva strain increases probability the most (LR = 14). For three of the maneuvers (squatting-to-standing, standing-to-squatting, passive leg elevation), the *absence* of the characteristic response decreases the probability of hypertrophic cardiomyopathy (LR = 0.1). Of these four maneuvers, only passive leg elevation can be easily performed in frail patients.

One other systolic murmur, mitral valve prolapse, may intensify during squatting-to-standing, although it does *not* become louder during Valsalva strain. This paradoxical finding, which is further discussed in Chapter 46, may explain why there are more false-positives for squatting-to-standing (specificity = 84%) than Valsalva strain (specificity = 95%).

(3). MANEUVERS CHANGING SYSTEMIC VASCULAR RESISTANCE (OR AFTERLOAD). Before using maneuvers that change afterload in diagnosing systolic murmurs, the clinician has already addressed the possibility of right-sided murmurs (respiratory maneuver) and hypertrophic cardiomyopathy (venous return maneuvers). The primary remaining diagnostic possibilities are murmurs generated by flow over the aortic valve (e.g., aortic stenosis or increased aortic flow without

‡ This occurs because pressures in the right side of the heart diminish with intrathoracic pressures during inspiration, increasing the pressure gradient between the right side of the heart and systemic veins and causing filling to increase to the right side of the heart. In contrast, inspiration increases the capacitance of pulmonary veins, thus reducing flow to the left side of the heart during inspiration.

EBM BOX 43.3
*Systolic Murmurs and Maneuvers**

Finding (Reference)†	*Sensitivity (%)*	*Specificity (%)*	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Respiration				
Louder During Inspiration				
Detecting right-sided murmurs (tricuspid regurgitation or pulmonic stenosis)[40,42]	78-95	87-97	7.8	0.2
Changing Venous Return				
Louder With Valsalva Strain				
Detecting hypertrophic cardiomyopathy[40]	70	95	14.0	0.3
Louder With Squatting-to-Standing				
Detecting hypertrophic cardiomyopathy[40]	95	84	6.0	0.1
Softer With Standing-to-Squatting				
Detecting hypertrophic cardiomyopathy[40,43]	88-95	84-97	7.6	0.1
Softer With Passive Leg Elevation				
Detecting hypertrophic cardiomyopathy[40]	90	90	9.0	0.1
Changing Systemic Vascular Resistance (Afterload)				
Softer With Isometric Hand Grip				
Detecting hypertrophic cardiomyopathy[40]	90	75	3.6	0.1
Louder With Isometric Hand Grip				
Detecting mitral regurgitation or ventricular septal defect[38,40]	70-76	78-93	5.8	0.3
Louder With Transient Arterial Occlusion				
Detecting mitral regurgitation or ventricular septal defect[40]	79	98	48.7	0.2
Softer With Amyl Nitrite Inhalation				
Detecting mitral regurgitation or ventricular septal defect[38,40,44,45]	41-95	89-95	10.5	0.2

*Diagnostic standard: Doppler echocardiography or angiography.
†Definition of findings: See text; for *amyl nitrite inhalation*, the test was interpretable only if it induced tachycardia.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
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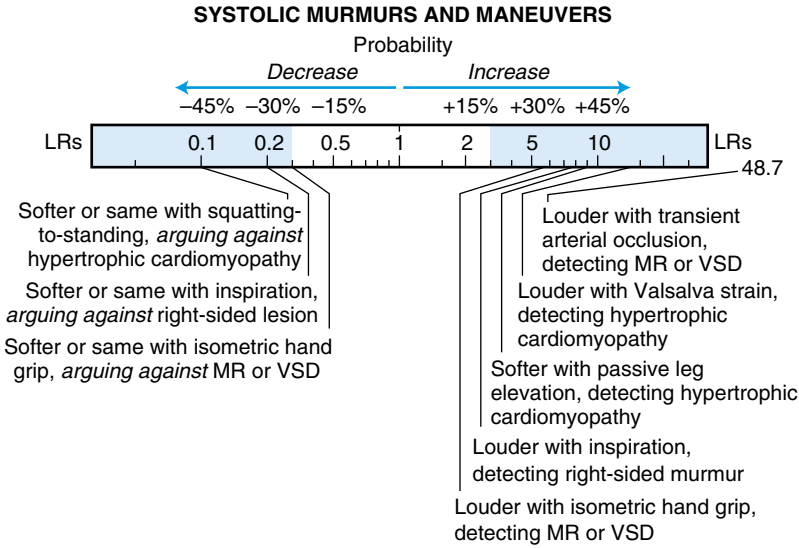

stenosis) and murmurs from left-sided regurgitant lesions (e.g., mitral regurgitation, ventricular septal defect).

Changing afterload may distinguish these lesions. The murmurs of mitral regurgitation and ventricular septal defect intensify with increased afterload because blood leaving the ventricle, having two paths to potentially follow, encounters more resistance in the aorta and therefore flows more readily through the regurgitant lesion. Similarly these murmurs become softer when afterload is decreased, because enhanced aortic flow reduces the regurgitant volume.

The common techniques of manipulating afterload at the bedside are isometric handgrip and transient arterial occlusion (see Table 43.3), both of which increase afterload. The finding of a systolic murmur that intensifies with either maneuver increases the probability of mitral regurgitation or ventricular septal defect (LR = 5.8 for isometric hand grip and 48.7 for transient arterial occlusion; see EBM Box 43.3). Another maneuver that reduces afterload, amyl nitrite inhalation, was used commonly 40 to 50 years ago but is rarely used today.

The references for this chapter can be found on www.expertconsult.com.

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